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| 10/574,046 | 01/31/2007 | Lynn Dickey | 040989/309915 | 9129 |

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| EXAMINER | |
|---|---|
| HISSONG, BRUCE D | |
| ART UNIT | PAPER NUMBER |
| 1646 | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/574,046 | DICKEY ET AL. | |
| | Examiner | Art Unit | |
| | Bruce D. Hissong, Ph.D. | 1646 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *08 June 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *30-34 and 90-99* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *30-34 and 90-99* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/8/2010*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

***Formal Matters***

1. Applicants' response to the office action mailed on 1/8/2010 was received on 6/8/2010 and has been entered into the record.

2. Claims 30-34 and 90-99 are currently pending and under examination.

***Information Disclosure Statement***

The information disclosure statement received on 6/8/2010 has been fully considered.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

1. Rejection of claims 30-34, 90-93, and 95-98 under 35 USC § 103(a) as being obvious in view of the combination of Franke *et al* (*DNA*, 1982, Vol. 1, p. 223-230) and Welcher *et al* (US 20050221344), as set forth on pages 6-8 of the office action mailed on 1/8/2010, is *withdrawn*.

In the response received on 6/8/2010, the Applicants argue that Franke teaches production of a delta-11 C-terminal truncation of IFN-α-2a, rather than the claimed IFN-α-2b. The Applicants also argue that Franke shows that C-terminally truncated IFN-α-2a polypeptides have activity that is unpredictable, and therefore there is nothing in the teachings of Franke to guide one of skill in the art to create C-terminally truncated IFN-α-2b variants. The Applicants also note that the polypeptide disclosed in Welcher is different from IFN-α-2b, and thus the disclosure of Welcher also does not provide motivation to create a C-terminally truncated IFN-α-2b polypeptide.

These arguments have been fully considered and are persuasive.

2. Rejection of claims 94 and 99 under 35 USC § 103(a) as being obvious in view of the combination of Franke *et al* (*DNA*, 1982, Vol. 1, p. 223-230), Welcher *et al* (US 20050221344), and Raskin (US 6,096,546), as set forth on pages 8-9 of the office action mailed on 1/8/2010, is *withdrawn*.

In the response received on 6/8/2010, the Applicants argue that the claims cannot be obvious in view of Franke for the reasons set forth above, and Raskin does not cure this deficiency.

These arguments have been fully considered and are persuasive.

*New Grounds of Rejection*

3. Claims 30-34, 90-93, and 95-98 are rejected under 35 U.S.C. 103(a) as being unpatentable over Levy *et al* ("Levy" – *Proc. Natl. Acad. Sci. USA*, 1981, Vol. 78, No. 10, p. 6186-6190), in view of Welcher *et al* ("Welcher – US 20050221344). Welcher was cited previously, and Levy was cited in the IDS received on 3/29/2006.

The claims of the present invention are drawn to isolated polynucleotides encoding the polypeptides consisting of SEQ ID NO: 5 or SEQ ID NO: 10, or alternatively SEQ ID NO: 10 operably linked to a signal peptide. The claims also recite an expression cassette comprising the isolated polynucleotides, and a host cell comprising said expression cassette, wherein said host cells are selected from mammalian cells, plant cells, insect cells, yeast cells, and prokaryotic cells.

Levy teaches IFN-α polypeptides, including carboxy-truncated polypeptides (see abstract), and an IFN-α polypeptide which is equivalent to IFN-α-2b (see Figure 4 – an examination of the sequence of Fig. 4 indicates that the sequence is identical to the sequence of SEQ ID NO: 11 except for the position 23, which is a lysine in Figure 4. However, Figure 4 also teaches that an arginine at position 23 may be representative of another IFN-α polypeptide; in this case, IFN-α-2b). Levy also teaches that mature IFN-α polypeptides are predicted to have 165 or 166 amino acids, but a significant portion of isolated IFN-α polypeptides lack the 10 C-terminal amino acids (p. 6186, 1st column, last full paragraph).

Welcher teaches IFN polypeptides which may be truncated at the carboxy terminus, and nucleic acids encoding such carboxy-terminated IFN polypeptides (paragraph 0073 and claim 3). Welcher also teaches truncated IFN polypeptides with leader or signal peptides (paragraphs 0175, 0177) and nucleic acids encoding IFN polypeptides with a signal peptide (paragraph 0359), wherein the nucleic acid sequence encoding said signal peptide is positioned at the 5' end of the IFN encoding region. Welcher

further discloses nucleic acids encoding truncated IFN with a vector (claim 4) and both prokaryotic and eukaryotic host cells comprising said vector (claims 5-7). Regarding host cells, Welcher teaches that appropriate host cells include bacterial (*E. coli* - paragraph 0188) and numerous mammalian cells (paragraph 0189), as well as plants (paragraphs 0193, 0213). Welcher also claims a process for preparing IFN polypeptides comprising culturing a host cell comprising a vector encoding an IFN polypeptide and isolating said polypeptide from the culture (claim 9).

Therefore, one of ordinary skill in the art, at the time the present invention was conceived, would have been motivated to create nucleic acid molecules encoding truncated IFN-α-2b polypeptides equivalent to the polypeptides of SEQ ID NO: 10 or SEQ ID NO: 5. The motivation to do so comes from the combined teachings of Levy, which teaches carboxy-truncated IFN-α-2b polypeptides, including carboxy-truncated IFN-α-2b which exhibits biological activity, and Welcher, which teaches truncation of IFN-like polypeptides and expression of said polypeptides. Although neither Levy nor Welcher specifically teaches the IFN-α polypeptides of SEQ ID NO: 5 or SEQ ID NO: 10, Levy teaches that IFN-α-2b polypeptides may be truncated by 10 amino acids at the C-terminus compared to the predicted polypeptide sequence, and therefore a person of ordinary skill in the art would be motivate to create additional IFN-α-2b polypeptides comprising other C-terminal truncations, such as a truncation of 8 amino acids, for the purpose of determining the effects of this region on various biological activities of IFN-α-2b. Therefore, one of ordinary skill in the art would be motivated to create polypeptides which are equivalent to the 8 amino acid C-terminal truncation of the mature IFN-α-2b of SEQ ID NO: 10, or the precursor polypeptide of SEQ ID NO: 5. When there is motivation to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try may show that it was obvious under § 103 (*KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 82 USPQ2d 1385, 1397 (2007)).

In the instant case, there is a finite number of amino acids within the carboxy-terminus region of IFN-α-2b, such as the carboxy-terminal 10 amino acids removed from the IFN-α of Levy. Furthermore, as set forth above, there is sufficient motivation provided by Levy to create additional IFN-α carboxy-terminated mutants for the purpose of studying the biological role of the carboxy-terminus. Therefore, it would be obvious to create nucleic acid encoding a carboxy-truncated mutant of IFN-α, which is truncated by 8 amino acids and which is equivalent to SEQ ID NO: 10. Furthermore, Welcher teaches carboxy-truncated mutants of both mature IFN (lacking a leader sequence) and IFN with a leader

sequence (paragraph 0077) with carboxy-truncations, and therefore a person of ordinary skill would also be motivated to create a nucleic acid encoding IFN-α with a leader sequence, wherein this polypeptide is truncated by 7 amino acids at the carboxy-terminus, and wherein this polypeptide would be equivalent to SEQ ID NO: 5.

Finally, because Welcher teaches nucleic acids encoding truncated IFN-α polypeptides, and vectors and host cells comprising these nucleic acids, including mammalian and plant host cells, and various signal peptides, one of ordinary skill in the art would be motivated to create nucleic acid molecules encoding the polypeptides of SEQ ID NOs 5 and 10, as discussed above, and would further be motivated to create expression vectors comprising these nucleic acids and host cells, including mammalian and plant host cells, for the purpose of expressing the IFN polypeptides.

2. Claims 94 and 99 are rejected under 35 U.S.C. 103(a) as being unpatentable over Levy *et al* ("Levy" – *Proc. Natl. Acad. Sci. USA*, 1981, Vol. 78, No. 10, p. 6186-6190), in view of Welcher *et al* ("Welcher" - US 20050221344), and further in view of Raskin (US 6,096,546).

The subject matter of the present invention and the teachings of Levy and Welcher are discussed above. Claims 94 and 99 are drawn to host cells comprising nucleic acids encoding the polypeptides of SEQ ID NOs 5 or 10, wherein said host cells are duckweed cells.

Levy teaches carboxy-truncated IFN-α-2b polypeptides, while Welcher teaches expression of IFN-like polypeptides in various host cells, including plant cells. Both Levy and Welcher are silent regarding expression of IFN polypeptides in duckweed. However, Raskin teaches expression of proteins in plants, and specifically teaches expression in duckweed (see claim 5, for example).

Therefore, one of ordinary skill in the art, at the time the present invention was conceived, would have been motivated to create nucleic acids encoding the carboxy-truncated IFN-α-2b polypeptides of SEQ ID NO: 5 or 10, and express these nucleotides in duckweed cells. The motivation to do so comes from the combined teachings of Levy and Welcher, which as discussed above, provide the motivation to create nucleic acids encoding the polypeptides of SEQ ID NOs 5 or 10 and express them in various host cells, including plant cells. Further motivation comes from Raskin, which teaches that duckweed cells are appropriate host cells for protein expression. Therefore, one of ordinary skill in the art would be motivated to express the nucleic acids suggested by Levy and Welcher in the duckweed cells taught by Raskin.

***Conclusion***

No claim is allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bruce D. Hissong, Ph.D., whose telephone number is (571)272-3324. The examiner can normally be reached M-F from 8:30 am - 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, Ph.D., can be reached at (571) 272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Bruce D. Hissong
Art Unit 1646

/Robert Landsman/
Primary Examiner, Art Unit 1647